ABSTRACT SUBMISSION

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Curvature-dependent epithelial tissue migration and orientation

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ABSTRACT

A large body of studies have highlighted that cells are sensitive to nanotopographies or geometrical cell-scale structures. However, natural biotopes also exhibit much larger topographical cues that are often curved and smooth, such as walls of blood vessels, bone cell cavities, or other cell bodies. Very little is known about how isolated cells and tissues read and integrate cell-scale curvatures, and the mechanisms leading to the integration of such physical cues. Herein we develop a two-step fabrication method to produce a series of edge-free cell-scale anisotropic sinusoidal landscapes with very low micro roughness. We employ these new model surfaces to investigate the epithelial cell layers' response to cell-scale curvature variations. We combine live imaging, biochemistry and modeling approaches to decipher integration mechanisms at the cellular and tissue levels.

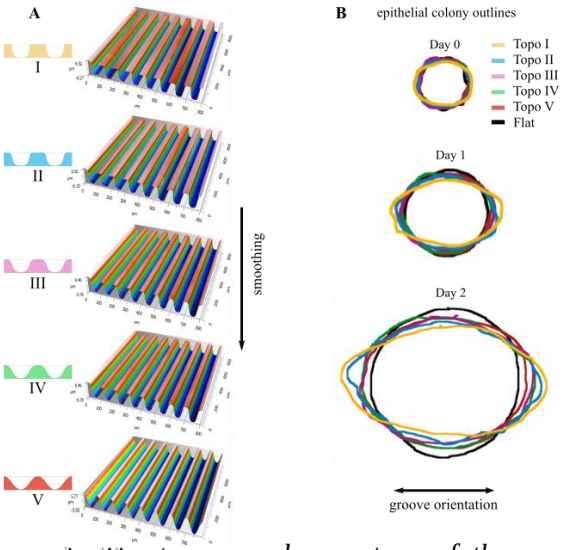

Figure 1: The transversal curvature of the topography controls the extent of anisotropic growth of the epithelial monolayer

Recently we report a new cellular sense which we term "curvotaxis" that enables the isolated cells to react to cell-scale curvature variations, a ubiquitous trait of cellular biotopes. We show that cells avoid convex regions during their migration and position themselves in concave valleys [1].

Here we report the curvature-modulated anisotropic growth of unconfined epithelia over cell-scale grooves and ridges of various transversal curvature. Curved regions of the substrate work as "topographical barriers", causing heterogeneity and reorientation of the nuclei and F-actin position. As a result, the epithelium displays a spatial bias in various morphogenetic processes such as migration or mitosis (Fig.1). Altogether, this work establishes cell-scale curvature as a major tuning parameter to regulate the growth of epithelia and opens new possibilities for tissue engineering research.

References : [1] Pieuchot L. et al. (2018) Nature Communications, 9:3995, doi: 10.1038/s41467-018-06494-6